39. (Amended) The method of claim 1, wherein each of the polymers further comprises a label [other than a monomer unit of the polymers].

REMARKS

I. Status of the Application

Claims 1-8, 10-15 and 37-39 are presently pending in the application. Claims 1-8, 10-15 and 37-39 stand rejected under 35 U.S.C. § 112, first paragraph for various reasons of record. Claims 1-7, 10, 12-15 and 37-39 stand rejected under 35 U.S.C. § 112, second paragraph for various reasons of record. Claims 1-8, 10-15 and 37-39 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Lam et al. US Patent No. 5,640,489 (102(e) date of at least 7/2/91) in view of Fodor et al. Science 251: 767 (1991) and applicants' disclosure of the prior art teachings. Claims 1-8, 10-15 and 37-39 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Lam et al. US Patent No. 5,640,489 (102(e) date of at least 7/2/91) in view of Holmes US Patent No. 5,679,773 and applicants' disclosure of the prior art teachings.

Applicants have amended the claims under consideration to more clearly define and distinctly characterize applicants' novel invention. Applicants' respectfully request entry and consideration of the foregoing amendments which are intended to place this case in condition for allowance.

II. The Rejection of the Claims Under 35 USC § 112, First and Second Paragraphs

In response to the Examiner's rejection of certain claims under 35 USC § 112 first paragraph, applicants have amended claim 39 to delete the phrase "other than a monomeric unit of the

polymers". Claims 1 and 10 have been amended to recite "measuring presence of diverse unbound polymers" which the Examiner has indicated is supported by the specification. Claims 3-5 have been amended to indicate that the labeled unbound polymers are heterogenous by number of monomeric units. Support for amendment appears at page 14 line 28 to page 15 line 24 which disclose that polymers are formed from monomer units. Claim 2 has been amended to recite "a single isomeric label". Support for the amendment is found at page 3 line 21-23 which discloses that the labeled polymers each typically comprise a single isomeric label.

Accordingly, applicants respectfully request that the Examiner withdraw his rejections to the claims under 35 USC § 112.

III. Claims 1-8, 10-15 and 37-39 are Patentable over Lam in view of Fodor

At page 8 paragraph 15, claims 1-8, 10-15 and 37-39 stand rejected under 35 USC §103(a) as being unpatentable over Lam et al. US Patent No. 5,640,489 in view of Fodor et al. Science 251: 767 (1991). The Examiner has stated that Lam et al. do not teach the formation of arrays on planar surfaces, where each member of the polymer set occupies a different region of the substrate. Instead, the Examiner has chosen to modify the method of Lam et al. with Fodor et al. which the Examiner states teaches the synthesis of polymer arrays on planar substrates where each member of the polymer array occupies a different region of the substrate. The Examiner concludes that one of ordinary skill in the art would be motivated to modify Lam et al. with Fodor to compare array synthesis protocols and optimize array synthesis (which is desirable whether the array has been prepared on a planar support or spherical supports, segmented supports, fiber supports . . . as each

are known in the art) as taught by Lam et al. The Examiner further states that Lam et al. teaches the desirability of monitoring polymer array synthesis in order to compare methods utilized in the synthetic process (Example 7) which is applicable to arrays synthesized on any support(s).

Applicants respectfully traverse the Examiner's rejection based on the amended claims now presented. Lam et al US Patent No. 5,650,489 fails to teach or suggest a method of monitoring polymer array synthesis on a solid substrate including (1) the formation of a preselected array of diverse polymers connected to cleavable linkers on a planar surface of solid substrate, whereby the diverse polymers occupy different regions of the substrate; (2) cleaving diverse polymers from the solid substrate by cleaving the cleavable linkers, thereby creating a mixture of diverse unbound polymers or (3) measuring presence of diverse unbound polymers as an indicator of the efficiency of the synthesizing step. Fodor et al. fails to cure the deficiencies of Lam et al.

Lam et al provides no motivation that it may be modified in the manner suggested by the Examiner. In fact, Lam et al. ***teaches against*** being modified by the teachings of Fodor et al.

Lam et al. teaches at col. 5 lines 19-24 (emphasis added)

> a method for determining the sequence of a bio-oligomer ligand for an acceptor molecule comprising the steps of generating a random library of bio-oligomer attached to solid supports ***wherein each solid phase support is attached to a single bio-oligomer species*** . . . .

In the Background of the Invention, Lam et al. identifies several approaches to the preparation of peptide libraries including Fodor et al. Regarding Fodor et al. Lam et al. states at col. 3 lines 48-52

> The method of Fodor et al., utilizes a "light-directed spatially addressable parallel chemical synthesis" technique. This technique is also limited by the relative lack of development of photochemical peptide synthesis methods.

Lam et al. also identify al col. 3 the method of Houghton which is directed to synthesizing hundreds of analogous peptides simultaneously in polypropylene mesh packets (tea bag method). At col. 4, Lam et al. further discloses that

> Although useful, as a practical matter the chemical techniques of Geysen, Fodor, Houghton, Berg and Furka and co-workers allow the synthesis and testing of only hundreds to a few thousand peptides at a time. These techniques are quite limited in light of the millions of possible peptide sequences, one or more of which might correspond to the binding sites between the entities of interest . . . . None of the procedures enable the synthesis of this many peptides at one time . . . .
>
> In addition, none of the other conventional peptide synthesis methods provide for the synthesis of a library of peptides bound to a solid phase support that is truly random. A truly random peptide library is one with a good statistical distribution of all the molecular species such that the library contains approximately equimolar ratios of all individual species of peptides.
>
> . . . . .
>
> In addition, none of the prior peptide synthesis methods provides for the synthesis of a library of greater than 10^5 peptides in which a single peptide species [is] attached to a single solid phase support. The representation of only one species on a solid support would greatly enhance current techniques for isolating peptides.
>
> Thus, there is a need in the art for a library of truly random peptide sequences, and oligonucleotide sequences, i.e., bio-oligomer sequences in which a single bio-oligomer species can be readily and quickly isolated from the rest of the library. There is also a need in the art for a method for quickly and inexpensively synthesizing thousands to millions of these truly random bio-oligomer sequences.

Based on the above disclosure in Lam et al., applicants respectfully submit that Lam et al. teaches against its combination with Fodor et al. Lam et al. very clearly sets forth its perceived limitations of Fodor et al. which discloses the production of an array on the surface of a solid support. Lam et al. overcomes its perceived limitations of Fodor et al. by using resin beads with each bead having a single bio-oligomer species. Example 7 of Lam et al is very clearly directed to the use

of resin beads onto which polymers are created (see reference to "solid phase supports") and not to a planar surface of a solid substrate whereby diverse polymers occupy different regions of the substrate. Based upon the disclosure in Lam et al., one of ordinary skill in the art would not be motivated to modify the methods of Lam et al. with the array of Fodor et al. since Lam et al. teaches the use of resin beads provide benefits and advantages that Lam et al. believes are not attainable by Fodor et al. In view of the disclosure of Lam et al., applicants' respectfully submit that the teachings of Lam et al. are not applicable to arrays synthesized on any support as urged by the Examiner. In fact, Lam teaches against the use of planar supports as not being able to achieve the important benefits and advantages of the resin beads used by Lam et al. with each bead having a single bio-oligomer species.

Accordingly, applicants respectfully request that the Examiner withdraw his rejection.

IV. Claims 1-8, 10-15 and 37-39 are Patentable over Lam in view of Holmes

At page 12 paragraph 17, claims 1-8, 10-15 and 37-39 stand rejected under 35 USC §103(a) as being unpatentable over Lam et al. US Patent No. 5,640,489 in view of Holmes US Patent No. 5,679,773. As stated above, Lam et al. fails to teach or suggest a method of monitoring polymer array synthesis on a solid substrate including (1) the formation of a preselected array of diverse polymers connected to cleavable linkers on a planar surface of solid substrate, whereby the diverse polymers occupy different regions of the substrate; (2) cleaving diverse polymers from the solid substrate by cleaving the cleavable linkers, thereby creating a mixture of diverse unbound polymers or (3) measuring presence of diverse unbound polymers as an indicator of the efficiency of the

synthesizing step. Holmes fails to cure the deficiencies of Lam et al. for the same reasons that Fodor fails to cure the deficiencies of Lam et al. Lam et al. teaches against modifying its resin beads with a planar substrate.

Accordingly, applicants respectfully request that the Examiner withdraw his rejection.

V. Conclusion

Having addressed all outstanding issues, applicants respectfully request entry and consideration of the foregoing amendments and reconsideration and allowance of the case. To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is requested to telephone the undersigned at the number below.

Respectfully submitted,

Dated: May 26, 2000

John P. Iwanicki
Reg. No. 34,628
BANNER & WITCOFF, LTD.
28 State Street, 28th Floor
Boston, MA 02109
(617) 227-7111